AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for screening a combination of treatments to specifically target a disease process that impacts gene expression, said method comprising the steps of:

(a) providing differential expression levels of predetermined genes of diseased tissue samples relative to at least one reference tissue for respective features of microarrays targeting the predetermined genes, wherein each feature targets a specific gene, said features being used to calculate the differential expression levels;

(b) for each of the respective features of respective microarrays for each diseased tissue sample, providing a single phenotypic/genotypic signature representing the differential expression level for each diseased tissue sample for that feature across the respective microarrays, ~~respectively~~;

(c) treating the diseased tissue samples with a treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment;

(e) generating a single phenotypic signature representing the treatment-response values of each of the diseased tissue samples;

(f) repeating steps (c) – (e) with a different treatment at least once so that multiple phenotypic signatures have been generated for multiple treatments;

(g) performing a clustering operation based on the phenotypic/genotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together; and

(h) selecting treatments by identifying the treatment-response phenotypic signatures caused by those treatments, and which are clustered with phenotypic signatures representing differential expression levels representative of the diseased tissue samples.

2. (Original) The method of claim 1, wherein said providing differential expression levels further comprises processing the diseased tissue samples and the at least one reference tissue using microarray technology to obtain the differential expression levels of the diseased tissues relative to the at least one reference tissue.

3. (Original) The method of claim 1, wherein said providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively, comprises generating the phenotypic/genotypic signatures based on the differential expression levels provided.

4. (Original) The method of claim 1, wherein each said treatment is selected from the group consisting of: a drug, a combination of drugs, a compound, a combination of compounds, radiation, a genetic sequence, a combination of genetic sequences, heat, cryogenics and a combination of two or more of any of the previous members in this group.

5. (Previously Presented) The method of claim 1, further comprising the steps of:

labeling the phenotypic/genotypic signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (g) and (h).

6. (Original) The method of claim 1, wherein said clustering operation includes finding a density center of a cluster, and calculating distances of the phenotypic signatures, belonging to the cluster, from the density center.

7. (Original) The method of claim 6, wherein the selection of treatments is made to address a broad spectrum of genes involved in the disease process of the diseased tissues.

8. (Original) The method of claim 7, wherein the treatments are selected by selecting treatment-response signatures within a cluster and having varying distances from the density center.

9. (Original) The method of claim 1, wherein said phenotypic signatures are normalized prior to said clustering.

10. (Original) The method of claim 5, wherein said phenotypic signatures are normalized prior to said clustering.

11. (Original) A method comprising forwarding a result obtained from the method of claim 1 to a remote location.

12. (Original) A method comprising transmitting data representing a result obtained from the method of claim 1 to a remote location.

13. (Original) A method comprising receiving a result obtained from a method of claim 1 from a remote location.

14. (Original) The method of claim 2, wherein said processing to obtain differential expression levels comprises processing a diseased-tissue sample and the reference tissue on a two-color, two channel microarray apparatus.

15. (Original) The method of claim 2, wherein said processing to obtain differential expression levels comprises processing a diseased-tissue sample on a single channel microarray apparatus, processing the reference tissue on a single channel microarray apparatus, and comparing the results of the processing.

16. (Original) The method of claim 1, wherein each treatment-response value comprises a concentration level or amount of the treatment used to block or retard the growth of the tissue by a predetermined percentage over a predetermined period of time after treatment.

17. (Original) The method of claim 1, wherein each treatment-response value comprises a value characterizing the amount of blocking or retardation of growth of the tissue over a predetermined period of time after treatment with a fixed amount of the treatment.

18. (Original) The method of claim 1, further comprising generating at least one phenotypic signature representing treatment-response values of each of the diseased tissue samples resultant from treating the diseased tissue samples with at least one treatment having known undesirable characteristics for treatment of the diseased tissues;

including that at least one phenotypic signature resulting from said treatment having known undesirable characteristics with all other signatures included in performing the clustering step (g); and

discarding any phenotypic signature representing treatment-response values from candidacy for the selection step (h) when the phenotypic signature is less than or equal to a predefined distance from a location of the at least one phenotypic signature resulting from treatment with a treatment having known undesirable characteristics.

19. (Original) The method of claim 18, wherein said known undesirable characteristics comprise an unacceptable level of toxicity.

20. (Original) The method of claim 18, wherein said known undesirable characteristics comprise an insufficient efficacy.

21. (Currently Amended) A method of augmenting an original or existing single treatment or treatment combination for a disease with at least one additional treatment that covers gene activity of the disease not addressed by the original or existing treatment, said method comprising the steps of:

(a) providing differential expression levels of predetermined genes of diseased tissue samples relative to at least one reference tissue for respective features of microarrays targeting the predetermined genes, wherein each feature targets a specific gene, said features being used to calculate the differential expression levels;

(b) for each of the respective features of respective microarrays for each diseased tissue sample, providing a phenotypic/genotypic signature representing the differential expression level for each diseased tissue sample for that feature across the respective microarrays~~, respectively~~;

(c) treating the diseased tissue samples with the original or existing single treatment or combination treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the original or existing single or combination treatment;

(e) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples as effected by the original or existing single or combination treatment;

(f) treating the diseased tissue samples with a treatment that is not included in the original or existing single or combination treatment;

(g) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment that is not included in the original or existing single or combination treatment;

(h) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples as effected by the treatment that is not included in the original or existing single or combination treatment;

(i) repeating steps (f) – (h) with a different treatment that is also not included in the original or existing single or combination treatment at least once so that multiple phenotypic signatures have been generated for multiple treatments not included in the original or existing single or combination treatment;

(j) performing a clustering operation based on the phenotypic/genotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together; and

(k) selecting at least one treatment by identifying the treatment-response phenotypic signatures caused by the at least one treatment, and which are clustered with phenotypic signatures identifying the treatment-response phenotypic signatures caused by the treatment or treatments in the original treatment, as well as with phenotypic signatures representing differential expression levels representative of the diseased tissue samples, but separated from the phenotypic signatures identifying the treatment-response phenotypic signatures caused by the treatment or treatments in the original treatment, so as to address disease-gene activity not currently addressed by the treatment or treatments in the original or existing treatment.

22. (Original) The method of claim 21, wherein each said treatment is selected from the group consisting of: a drug, a combination of drugs, a compound, a combination of compounds, radiation, a genetic sequence, a combination of genetic sequences, heat, cryogenics and a combination of two or more of any of the previous members in this group.

23. (Previously Presented) The method of claim 21, further comprising the steps of:

labeling the phenotypic/genotypic signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (j) and (k).

Claims 24-29. (Canceled)

30. (Original) A method for determining phase relationships between treatment responses of diseased tissues to treatments which are applied thereto and expression profiles of the diseased tissues, said method comprising the steps of:

(a) providing differential expression levels of predetermined genes of the diseased tissue samples relative to at least one reference tissue for respective features of microarrays targeting the predetermined genes used to calculate the differential expression levels;

(b) for each of the respective features on respective microarrays for each disease tissue sample, providing a phenotypic signature representing the differential expression level for each diseased tissue sample for that feature across the respective microarrays, ~~respectively~~;

(c) treating the diseased tissue samples with a treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment;

(e) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples;

(f) comparing the treatment-response phenotypic signature with the differential expression level phenotypic signatures for similarity; and

(g) targeting gene profiles effected by the treatment based upon the similarity results.

31. (Original) The method of claim 30, wherein said providing differential expression levels further comprises processing the diseased tissue samples and the at least one reference tissue using microarray technology to obtain the differential expression levels of the diseased tissues relative to the at least one reference tissue.

32. (Original) The method of claim 30, wherein said providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively, comprises generating the phenotypic/genotypic signatures based on the differential expression levels provided.

33. (Original) The method of claim 30, wherein each said treatment is selected from the group consisting of: a drug, a combination of drugs, a compound, a combination of compounds, radiation, a genetic sequence, a combination of genetic sequences, heat, cryogenics and a combination of two or more of any of the previous members in this group.

34. (Previously Presented) The method of claim 30, further comprising the steps of:

labeling the phenotypic/genotypic signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (f) and (g).

Claims 35-41. (Canceled)

42. (New) A method for screening a combination of treatments to specifically target a disease process that impacts gene expression, said method comprising the steps of:

(a) providing differential expression levels of predetermined genes of diseased tissue samples relative to at least one reference tissue for respective features of microarrays targeting the predetermined genes used to calculate the differential expression levels;

(b) for each of the respective features of respective microarrays for each diseased tissue sample, providing a single phenotypic/genotypic signature as a vector representing the differential expression level for each diseased tissue sample for that feature across the respective microarrays;

(c) treating the diseased tissue samples with a treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment;

(e) generating a single phenotypic signature as a response vector representing the treatment-response values of each of the diseased tissue samples;

(f) repeating steps (c) – (e) with a different treatment at least once so that multiple phenotypic signatures have been generated for multiple treatments;

(g) performing a clustering operation based on the phenotypic/genotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together;

(h) selecting treatments by identifying the treatment-response phenotypic signatures caused by those treatments, and which are clustered with phenotypic signatures representing differential expression levels representative of the diseased tissue samples;

(i) labeling the phenotypic/genotypic signatures representing the differential expression levels as "in phase" signatures;

(j) generating "out of phase" signatures by inverting the "in phase" signatures; and

(k) including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (g) and (h).

43. (New) A method of augmenting an original or existing single treatment or treatment combination for a disease with at least one additional treatment that covers gene activity of the disease not addressed by the original or existing treatment, said method comprising the steps of:

(a) providing differential expression levels of predetermined genes of diseased tissue samples relative to at least one reference tissue for respective features of microarrays targeting the predetermined genes used to calculate the differential expression levels;

(b) for each of the respective features of respective microarrays for each diseased tissue sample, providing a phenotypic/genotypic signature as a vector representing the differential expression level for each diseased tissue sample for that feature across the respective microarrays;

(c) treating the diseased tissue samples with the original or existing single treatment or combination treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the original or existing single or combination treatment;

(e) generating a phenotypic signature as a vector representing the treatment-response values of each of the diseased tissue samples as effected by the original or existing single or combination treatment;

(f) treating the diseased tissue samples with a treatment that is not included in the original or existing single or combination treatment;

(g) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment that is not included in the original or existing single or combination treatment;

(h) generating a phenotypic signature as a vector representing the treatment-response values of each of the diseased tissue samples as effected by the treatment that is not included in the original or existing single or combination treatment;

(i) repeating steps (f) – (h) with a different treatment that is also not included in the original or existing single or combination treatment at least once so that multiple phenotypic signatures have been generated for multiple treatments not included in the original or existing single or combination treatment;

(j) performing a clustering operation based on the phenotypic/genotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together;

(k) selecting at least one treatment by identifying the treatment-response phenotypic signatures caused by the at least one treatment, and which are clustered with phenotypic signatures identifying the treatment-response phenotypic signatures caused by the treatment or treatments in the original treatment, as well as with phenotypic signatures representing differential expression levels representative of the diseased tissue samples, but separated from the phenotypic signatures identifying the treatment-response phenotypic signatures caused by the treatment or treatments in the original treatment, so as to address disease-gene activity not currently addressed by the treatment or treatments in the original or existing treatment;

labeling the phenotypic/genotypic signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (j) and (k).